

WHAT IS CLAIMED IS:

1. An adhesive composition comprising:
a polymerizable 1,1-disubstituted ethylene monomer; and
at least one stabilizer selected from the group consisting of herbal
5 extracts, alpha- and beta- hydroxycarboxylic acids and salts thereof, ceramides, anti-
inflammatories, vasoconstrictors, and mixtures thereof.
2. The composition of claim 1, wherein said stabilizer is an herbal extract.
3. The composition of claim 2, wherein said herbal extract is an oil-
soluble herbal extract.
- 10 4. The composition of claim 3, wherein said herbal extract is selected
from the group consisting of chamomile, carrot root, echinacea purpurea, fennel,
ginseng, grape seed, grape skin, grapefruit, guggalipids, harpogophytum, jasmine,
marjoram, myrrh gum resin, onion, pine bark, red clover flower, resveratrol, rosemary,
sesame, St. Johns wort, thyme, Uva Ursi (bearberry), borage seed oil, wild borage
15 seed oil, hesperedin, quercetin, kaempherol, genistein, coumestrol, estriol,
phytosterols, limonene, ethoxyquin, hydroquinone, ubiquinone (coenzyme Q), lipoic
acid, N-acetyl cysteine, curcumin, basil leaf, bell pepper, dandelion root, date palm
fruit, licorice, tomato, myricetin, derivatives thereof, and mixtures thereof.
- 20 5. The composition of claim 3, wherein said herbal extract is selected
from the group consisting of chamomile, carrot root, echinacea purpurea, fennel,
ginseng, grape seed, grape skin, grapefruit, guggalipids, harpogophytum, jasmine,
marjoram, myrrh gum resin, onion, pine bark, red clover flower, resveratrol, rosemary,
sesame, St. Johns wort, thyme, Uva Ursi (bearberry), borage seed oil, wild borage
seed oil, hesperedin, quercetin, kaempherol, genistein, coumestrol, estriol,
25 phytosterols, limonene, ethoxyquin, hydroquinone, ubiquinone (coenzyme Q), lipoic
acid, N-acetyl cysteine, curcumin, derivatives thereof, and mixtures thereof.
6. The composition of claim 3, wherein said herbal extract is selected
from the group consisting of dill, horseradish, oats, neem, beet, broccoli, tea,
pumpkin, soybean, barley, walnut, flax, ginseng, poppy, avocado, pea, sesame,
30 dandelion, wheat, nettle, cashew, pineapple, apple, asparagus, Brazilnut, chickpea,
grapefruit, orange, cucumber, buckwheat, strawberry, ginko, tomato, blueberry,
cowpea, grape extracts, ivy horse chestnut, centella asiatica, rosmarinic acid,
glycyrrizinate derivatives, alpha bisabolol, azulene, asiaticoside, sericoside,

ruscogenin, escin, escolin, betulinic acid, catechin, derivatives thereof, and mixtures thereof.

7. The composition of claim 1, wherein said stabilizer is curcumin or a curcumin derivative.

5 8. The composition of claim 7, wherein said stabilizer is selected from the group consisting of curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin, tetrahydrodemethoxycurcumin, tetrahydrobisdemethoxycurcumin, other curcumin metabolites, (4-hydroxy-3-methoxycinnamoyl)methane, bis(4-hydroxycinnamoyl)methane, hexahydrocurcumin,
10 octahydrocurcumin, and mixtures thereof.

9. The composition of claim 1, wherein said stabilizer is an alpha- or beta-C₁-C₃₀ hydroxycarboxylic acid or salt thereof.

10. The composition of claim 9, wherein said stabilizer is selected from the group consisting of alpha- and beta-C₁-C₃₀ hydroxycarboxylic acids and salts thereof.

15 11. The composition of claim 9, wherein said stabilizer is selected from the group consisting of salicylic acid, alpha hydroxy acetic acid, alpha hydroxybenzeneacetic acid, alpha hydroxypropionic acid, alpha hydroxybutanoic acid, alpha hydroxyhexanoic acid, alpha hydroxyoctanoic acid, alpha hydroxynonanoic acid, alpha hydroxydecanoic acid, alpha hydroxyundecanoic acid, alpha
20 hydroxydodecanoic acid, alpha hydroxytetradecanoic acid, alpha hydroxyhexadecanoic acid, alpha hydroxyoctadecanoic acid, alpha hydroxyoctacosanoic acid, dicarboxylic alpha hydroxy acids, dihydroxybutanedioic acid (tartaric acid), 2-hydroxybutanedioic acid, 2-hydroxy propanedioic acid, 2-hydroxy hexanedioic acid, 2-hydroxy octanedioic acid, 2-hydroxy decanedioic acid,
25 2-hydroxy dodecanedioic acid, 2-hydroxy myristicdioic acid, 2-hydroxy palmiticdioic acid, tricarboxylic alpha hydroxy acid, 2-hydroxy-1,2,3,-propanetricarboxylic acid, 1-hydroxy-1,2,3-propanetricarboxylic acid, and mixtures thereof.

12. The composition of claim 1, wherein said stabilizer is a ceramide.

13. The composition of claim 12, wherein said ceramide is selected from
30 the group consisting of Ceramide 1, Ceramide 3, Ceramide 6, and mixtures thereof.

14. The composition of claim 1, wherein said stabilizer is an anti-inflammatory.

15. The composition of claim 14, wherein said anti-inflammatory is selected from the group consisting of beta-methasone 17-acetate, indomethacin,

ketoprofen, flufenamic acid, ibuprofen, diclofenace, diflunisal, fenclofenac, naproxen, piroxidam, sulindac, and mixtures thereof.

16. The composition of claim 1, wherein said stabilizer is a vasoconstrictor.

5 17. The composition of claim 16, wherein said vasoconstrictor is selected from the group consisting of papaverine, yohimbine, visnadin, khellin, bebellin, nicotinate derivatives, and mixtures thereof.

18. The composition of claim 1, wherein said monomer is an α -cyanoacrylate.

10 19. The composition of claim 1, wherein said monomer is at least one member selected from the group consisting of methyl cyanoacrylate, ethyl cyanoacrylate, n-butyl cyanoacrylate, 2-octyl cyanoacrylate, methoxyethyl cyanoacrylate, ethoxyethyl cyanoacrylate, hexyl cyanoacrylate, dodecyl cyanoacrylate, butyl lactoyl cyanoacrylate, butyl glycoloyl cyanoacrylate, ethyl lactoyl cyanoacrylate, and ethyl glycoloyl cyanoacrylate.

15 20. The composition of claim 1, wherein said stabilizer is present in said composition in a concentration of from about 0.01 to about 10.0% by weight.

21. The composition of claim 1, wherein said stabilizer is present in said composition in a concentration of from about 0.01 to about 5.0 % by weight.

20 22. The composition of claim 1, wherein said composition has a Sterility Assurance Level of not better than 10^{-3} .

23. The composition of claim 1, wherein said composition is sterilized to a Sterility Assurance Level of at least 10^{-3} .

25 24. The composition of claim 1, further comprising a non-stabilizer medicament.

25. The composition of claim 1, further comprising a plasticizer.

26. The composition of claim 1, wherein said stabilizer is present in an amount sufficient to stabilize said composition during sterilization.

30 27. The composition of claim 1, wherein said stabilizer is present in an amount sufficient to stabilize said composition during and subsequent to sterilization.

28. The composition of claim 1, wherein said stabilizer is present in an amount effective to provide wound healing when said composition is applied to a tissue surface.

29. The composition of claim 1, wherein said composition further comprises at least one antioxidant stabilizer.

30. The composition of claim 29, wherein said at least one antioxidant stabilizer is selected from the group consisting of vitamin E and derivatives thereof, vitamin K and derivatives thereof, vitamin C, pentamethyl chromanol, non-phenolic antioxidants, octyl gallate, and pentamethylbenzofuranol.

31. The composition of claim 29, wherein said at least one antioxidant stabilizer is pentamethyl chromanol.

32. A method of making the adhesive composition of claim 1, comprising combining the polymerizable 1,1-disubstituted ethylene monomer and the stabilizer.

33. A method of making a sterile polymerizable 1,1-disubstituted monomer adhesive composition comprising:

dispensing the polymerizable 1,1-disubstituted monomer adhesive composition of claim 1 into a container;

sealing said container; and

sterilizing the composition in the container.

34. A method of making a sterile polymerizable 1,1-disubstituted monomer adhesive composition comprising:

dispensing a polymerizable 1,1-disubstituted monomer adhesive composition into a container;

sealing said container; and

sterilizing the composition in the container to a Sterility Assurance

Level of at least 10^{-3} ,

wherein said polymerizable 1,1-disubstituted monomer composition comprises:

a polymerizable 1,1-disubstituted ethylene monomer; and

at least one stabilizer selected from the group consisting of herbal extracts, alpha- and beta- hydroxycarboxylic acids and salts thereof, ceramides, anti-inflammatories, vasoconstrictors, and mixtures thereof.

35. The method of claim 34, wherein said sterilizing is by dry heat, gamma irradiation, electron beam irradiation, or microwave irradiation.

36. The method of claim 34, wherein said sterilizing is by electron beam irradiation.

37. The method of claim 34, wherein said sterilizing is by gamma irradiation.

38. The method of claim 34, wherein the sterilized composition has a viscosity less than 150% of a viscosity of said composition prior to sterilizing.

5 39. The method of claim 34, wherein said stabilizer is an herbal extract.

40. The method of claim 39, wherein said herbal extract is an oil-soluble herbal extract.

41. The method of claim 40, wherein said herbal extract is selected from the group consisting of chamomile, carrot root, echinacea purpurea, fennel, ginseng, grape seed, grape skin, grapefruit, guggalipids, harpogophytum, jasmine, marjoram, myrrh gum resin, onion, pine bark, red clover flower, resveratrol, rosemary, sesame, St. Johns wort, thyme, Uva Ursi (bearberry), borage seed oil, wild borage seed oil, hesperedin, quercetin, kaempferol, genistein, coumestrol, estriol, phytosterols, limonene, ethoxyquin, hydroquinone, ubiquinone (coenzyme Q), lipoic acid, N-acetyl
10 cysteine, curcumin, basil leaf, bell pepper, dandelion root, date palm fruit, licorice, tomato, myricetin, derivatives thereof, and mixtures thereof.

42. The method of claim 40, wherein said herbal extract is selected from the group consisting of chamomile, carrot root, echinacea purpurea, fennel, ginseng, grape seed, grape skin, grapefruit, guggalipids, harpogophytum, jasmine, marjoram, myrrh gum resin, onion, pine bark, red clover flower, resveratrol, rosemary, sesame, St. Johns wort, thyme, Uva Ursi (bearberry), borage seed oil, wild borage seed oil, hesperedin, quercetin, kaempferol, genistein, coumestrol, estriol, phytosterols, limonene, ethoxyquin, hydroquinone, ubiquinone (coenzyme Q), lipoic acid, N-acetyl
20 cysteine, curcumin, derivatives thereof, and mixtures thereof.

43. The method of claim 40, wherein said herbal extract is selected from the group consisting of dill, horseradish, oats, neem, beet, broccoli, tea, pumpkin, soybean, barley, walnut, flax, ginseng, poppy, avocado, pea, sesame, dandelion, wheat, nettle, cashew, pineapple, apple, asparagus, Brazilnut, chickpea, grapefruit, orange, cucumber, buckwheat, strawberry, ginko, tomato, blueberry, cowpea, grape
30 extracts, ivy horse chestnut, centella asiatica, rosmarinic acid, glycyrrizinate derivatives, alpha bisabolol, azulene, asiaticoside, sericoside, ruscogenin, escin, escolin, betulinic acid, catechin, derivatives thereof, and mixtures thereof.

44. The method of claim 34, wherein said stabilizer is curcumin or a curcumin derivative.

45. The method of claim 44, wherein said stabilizer is selected from the group consisting of curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin, tetrahydrodemethoxycurcumin, tetrahydrobisdemethoxycurcumin, other curcumin metabolites, (4-hydroxy-3-methoxycinnamoyl)methane, bis(4-hydroxycinnamoyl)methane, hexahydrocurcumin, octahydrocurcumin, and mixtures thereof.

46. The method of claim 34, wherein said stabilizer is an alpha- or beta- $C_{1-C_{30}}$ hydroxycarboxylic acid or salt thereof.

47. The method of claim 46, wherein said stabilizer is selected from the group consisting of alpha- and beta- $C_{1-C_{30}}$ hydroxycarboxylic acids and salts thereof.

48. The method of claim 46, wherein said stabilizer is selected from the group consisting of salicylic acid, alpha hydroxy acetic acid, alpha hydroxybenzeneacetic acid, alpha hydroxypropionic acid, alpha hydroxybutanoic acid, alpha hydroxyhexanoic acid, alpha hydroxyoctanoic acid, alpha hydroxynonanoic acid, alpha hydroxydecanoic acid, alpha hydroxyundecanoic acid, alpha hydroxydodecanoic acid, alpha hydroxytetradecanoic acid, alpha hydroxyhexadecanoic acid, alpha hydroxyoctadecanoic acid, alpha hydroxyoctaicosanoic acid, dicarboxylic alpha hydroxy acids, dihydroxybutanedioic acid (tartaric acid), 2-hydroxybutanedioic acid, 2-hydroxy propanedioic acid, 2-hydroxy hexanedioic acid, 2-hydroxy octanedioic acid, 2-hydroxy decanedioic acid, 2-hydroxy dodecanedioic acid, 2-hydroxy myristicdioic acid, 2-hydroxy palmiticdioic acid, tricarboxylic alpha hydroxy acid, 2-hydroxy-1,2,3,-propanetricarboxylic acid, 1-hydroxy-1,2,3-propanetricarboxylic acid, and mixtures thereof.

49. The method of claim 34, wherein said stabilizer is a ceramide.

50. The method of claim 49, wherein said ceramide is selected from the group consisting of Ceramide 1, Ceramide 3, Ceramide 6, and mixtures thereof.

51. The method of claim 34, wherein said stabilizer is an anti-inflammatory.

52. The method of claim 51, wherein said anti-inflammatory is selected from the group consisting of beta-methasone 17-acetate, indomethacin, ketoprofen, flufenamic acid, ibuprofen, diclofenace, diflunisal, fenclofenac, naproxen, piroxidam, sulindac, and mixtures thereof.

53. The method of claim 34, wherein said stabilizer is a vasoconstrictor.

54. The method of claim 53, wherein said vasoconstrictor is selected from the group consisting of papaverine, yohimbine, visnadin, khellin, bebellin, nicotinate derivatives, and mixtures thereof.

55. The method of claim 34, wherein said monomer is an α -cyanoacrylate.

5 56. The method of claim 34, wherein said monomer is at least one member selected from the group consisting of methyl cyanoacrylate, ethyl cyanoacrylate, n-butyl cyanoacrylate, 2-octyl cyanoacrylate, methoxyethyl cyanoacrylate, ethoxyethyl cyanoacrylate, hexyl cyanoacrylate, dodecyl cyanoacrylate, butyl lactoyl cyanoacrylate, butyl glycoloyl cyanoacrylate, ethyl lactoyl cyanoacrylate, and ethyl glycoloyl
10 cyanoacrylate.

57. The method of claim 34, wherein said stabilizer is present in said composition in a concentration of from about 0.01 to about 10.0% by weight.

58. The method of claim 34, wherein said stabilizer is present in said composition in a concentration of from about 0.01 to about 5.0 % by weight.

15 59. The method of claim 34, wherein said composition has a total volume in said container of less than 10 milliliters.

60. The method of claim 34, wherein said composition further comprises at least one antioxidant stabilizer.

20 61. The method of claim 60, wherein said at least one antioxidant stabilizer is selected from the group consisting of vitamin E and derivatives thereof, vitamin K and derivatives thereof, vitamin C, pentamethyl chromanol, non-phenolic antioxidants, octyl gallate, and pentamethylbenzofuranol.

62. The method of claim 60, wherein said at least one antioxidant stabilizer is pentamethyl chromanol.

25 63. A sterile composition made by the method of claim 34.

64. A polymerized film made by polymerizing the composition of claim 1.

65. A method of treating tissue comprising:
applying the composition of claim 1 to tissue; and
allowing the monomer to polymerize to form a polymer film.

30 66. The method of claim 65, wherein said stabilizer is present in said polymer film in an amount effective to promote wound healing.